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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/825,584	04/04/2001	Robert Akita	P1003R1C1D1	3718

7590 11/05/2003

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EXAMINER	
YAEN, CHRISTOPHER H	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 11/05/2003

14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/825,584	AKITA ET AL.	
	Examiner	Art Unit	
	Christopher H Yaen	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-33 and 36-51* is/are rejected.

7)☐ Claim(s) *34 and 35* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The amendment filed 1/21/2003 (paper no. 13) is acknowledged and entered into the record. Accordingly, no claims have been canceled or added.

2. Claims 22-51 are therefore pending and examined on the merits.

Information Disclosure Statement

3. The Information Disclosure Statement filed 1/27/2003 (paper no. 11) is acknowledged and considered. A signed copy of the IDS is attached hereto.

New Arguments

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 22-33, and 36-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rajkumar T *et al* (Br. J. Cancer 1994;70:459-465, IDS 39) in view of Orlandi et al (Proc. Natl. Acad. Sci. USA, 86:3833-3837, 1989), Cabilly et al (U.S Patent 4816567, issued 3/89), Boss et al (U.S Patent 4816397, issued 3/89), Robinson et al (U.S. Patent 5618920, filed 4/94), Ward et al (Nature 341:544-546, 1989), Queen et al (PNAS 1989;86:10029-33) and Huston et al (U.S. Patent 5258498, issued 11/93).

The claims recite an isolated nucleic acid molecule that encodes an antibody that binds to ErbB3 (claim 22), wherein the antibody is a monoclonal antibody (claim 25), humanized (claim 26), human (claim 27), an antibody fragment comprising the antigen binding region (claim 28), and an Fab (claim 29). The claims are further limited to an isolated nucleic acid molecule that encodes an antibody capable of binding to ErbB3, wherein the antibody is capable of reducing or inducing the heregulin-induced ErbB2 activation (claim 23,24,30,31,32,33). The claims are also drawn to a vector comprising the said isolated nucleic acid (claims 36,40, 44,48), a host cell comprising the said vector (claims 37,41,45,49), a method of making an antibody comprising culturing the said host cell so as to express the nucleic acid (claims 38, 42, 46,50), and a method of conjugating to the produced antibody a cytotoxic agent or enzyme (claims 39,43,47,51).

Rajkumar *et al* teach the anti-ErbB3 antibody, hybridomas producing the said antibodies and the motivation to conjugate to toxins or enzymes (see page 464). Rajkumar *et al* further indicate that ErbB3 is able to bind to and be stimulated by heregulin (see page 459). Rajkumar *et al* do not teach isolated nucleic acid molecule encoding the ErbB3 antibodies, humanized antibodies, human antibodies, or antibody

fragments, the vectors, the host cells, or the methods of production. These deficiencies are made up for in the teachings of Orandi et al, Cabilly et al, Boss et al, Robinson et al, and Ward et al and Huston et al.

Orlandi et al teach a general method for obtaining the VH and the VL genes and the amino acid sequence of an antibody by PCR from the hybridoma cell. Orlandi also teaches primers and the use of said primers to clone DNA encoding murine variable heavy regions (see page 3833 and 3834) and the method obtained the sequences for five of the hybridomas for which it was applied.

Robinson et al (see columns 12-22) and Ward et al (see entire document) teach Fv derived from a known antibody. Robinson et al teach Fv, determination of nucleic acids encoding VH and VL of any known antibody and use of said VH and VL to produce FV (see column 1-45, and columns 12-22). Robinson et al teach that "The invention also produces consensus sequences and specific oligonucleotide sequences useful as probes for hybridization and priming cDNA synthesis of any hybridoma mRNA coding for variable regions of any desired specificity." (see column 4, last paragraph). Ward et al teach vectors for producing FV.

Both Cabilly et al and Boss et al disclose methods for the determination of nucleic acids encoding VH and VL of any known antibody.

Queen *et al* disclose a method of "humanizing" a anti-Tac antibody by combining the CDRs of the anti-Tac antibody with human framework regions.

Huston et al teach that the sequence of the VH and VL of a known antibody can be determined by amino acid sequencing and "The 5' end portion of the mRNA can be

used to produce the cDNA for subsequent sequencing or the amino acid sequence of the hypervariable and flanking framework regions can be determined by amino acid sequencing of the V regions of the H and L chains. Such sequence analysis is now conducted routinely".

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have used and obtain the nucleic acid sequence encoding anti-ErbB3 antibody as taught by Rajkumar *et al* by the method of Orlandi et al, Cabilly et al, Boss et al, Robinson et al, Ward et al and Huston et al, and use the method of taught by Rajkumar *et al* to conjugate the said antibody to a cytotoxic agent or to an enzyme, and use the method of Queen *et al* to produce humanized antibodies and to use the method of Robinson *et al* to produce human antibodies and to produce said antibody by using culturing the host cell comprising a vector comprising the isolated nucleic acids molecules encoding the said antibody.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have used the anti-ErbB3 antibody and obtain the nucleic acid sequence from the hybridoma as taught by Rajkumar *et al* by the method of Orlandi et al, Cabilly et al, Boss et al, Robinson et al, and Ward et al and Huston et al and the method of producing the antibodies by Robinson *et al* and use the method of Queen *et al* to produce the humanized antibodies because Rajkumar *et al* teach that the anti-ErbB3 antibodies would be useful as a therapeutic because of the specific overexpression of ErbB3 in many tumor types (see page 464).

As taught by Orlandi et al it was routine to obtain the VH and the VL genes from PCR primers from the hybridoma of an antibody and "our primers might amplify most immunoglobulin mRNA of the mouse repertoire" (see page 3836, right column) and "the teachings should lead to the cloning of antigen-binding specificities directly from immunoglobulin genes" (see abstract, last sentence). Cabilly et al teach that regarding VH and VL nucleic acid sequences that, "the variable regions can conveniently be derived from presently known sources using readily available hybridomas" (see column 6, last paragraph). Robinson et al teach that "The invention also produces consensus sequences and specific oligonucleotide sequences useful as probes for hybridization and priming cDNA synthesis of any hybridoma mRNA coding for variable regions of any desired specificity." (see column 4, last paragraph). Huston et al teach "The invention also produces consensus sequences and specific oligonucleotide sequences useful as probes for hybridization and priming cDNA synthesis of any hybridoma mRNA coding for variable regions of any desired specificity." (see column 4, last paragraph). Thus, the art recognized that there was a reasonable expectation of success that the nucleic acid sequence of the anti-ErbB3 antibody could be established using techniques disclosed in the references used in the instant rejection. As taught by Rajkumar *et al* the anti-ErbB3 antibody is able to bind to ErbB3 with specificity and as taught by Rajkumar *et al* it was known that Heregulin was able to bind to and stimulate ErbB3 activity. One of ordinary skill in the art would reasonably conclude that Rajkumar *et al*'s antibody would also be able to also reduce or induce heregulin induced ErbB2 activity. Since the Patent and Trademark Office does not have the facilities for examining and

comparing the claimed antibody with the antibody of Rajkumar *et al et al* or the nucleic acids which encode the antibodies, the burden of proof is upon the Applicants to show an unobvious distinction between the structural and functional characteristics of the claimed antibody and the antibody of the prior art. See In re Best, 562 F.2d 1252, 195 U.S.P.Q. 430 (CCPA 197) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

All other rejections are withdrawn in view of the arguments made thereto in paper no. 13.

Conclusion

6. Claims 34 and 35 appear to be free of the prior art. Claims 34 and 35 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

7. All other claims are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 703-305-3586. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Christopher Yaen
Art Unit 1642
August 27, 2003

ANTHONY C. CAPUTA
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